

ment the BLAST and BLAZE algorithms (Altschul et al., *J. Mol. Biol.* 215: 403-410 (1990)) can be used to identify open frames within the nucleic acid molecules of the present invention. A skilled artisan can readily recognize that any one of the publicly available homology search programs can be used as the search means for the computer-based systems of the present invention.

#### Uses of the Agents of the Present Invention

**[0211]** Nucleic acid molecules and fragments thereof of the present invention may be employed to obtain other nucleic acid molecules from other species. Such nucleic acid molecules include the nucleic acid molecules that encode the complete coding sequence of a protein and promoters and flanking sequences of such molecules. In addition, such nucleic acid molecules include nucleic acid molecules that encode for other isozymes or gene family members. Such molecules can be readily obtained by using the above-described nucleic acid molecules or fragments thereof to screen cDNA or genomic libraries obtained from *D. v. virgifera*. Methods for forming such libraries are well known in the art.

**[0212]** Nucleic acid molecules and fragments thereof of the present invention may also be employed to obtain other nucleic acid molecules such as nucleic acid homologues. Such homologues include the nucleic acid molecules that encode, in whole or in part, protein homologues of other species, plants or other organisms. Such molecules can be readily obtained by using the above-described nucleic acid molecules or fragments thereof to screen cDNA or genomic libraries. Methods for forming such libraries are well known in the art. Such homologue molecules may differ in their nucleotide sequences from those found in one or more of SEQ ID NO:1 through SEQ ID NO:9112 or complements thereof because complete complementarity is not needed for stable hybridization. The nucleic acid molecules of the present invention therefore also include molecules that, although capable of specifically hybridizing with the nucleic acid molecules may lack "complete complementarity." In a particular embodiment, methods or 3' or 5' RACE may be used to obtain such sequences (Frohman, M. A. et al., *Proc. Natl. Acad. Sci. (U.S.A.)* 85:8998-9002 (1988); Ohara, O. et al., *Proc. Natl. Acad. Sci. (U.S.A.)* 86:5673-5677 (1989)).

**[0213]** Any of a variety of methods may be used to obtain one or more of the above-described nucleic acid molecules (Zamechik et al., *Proc. Natl. Acad. Sci. (U.S.A.)* 83: 4143-4146 (1986); Goodchild et al., *Proc. Natl. Acad. Sci. (U.S.A.)* 85: 5507-5511 (1988); Wickstrom et al., *Proc. Natl. Acad. Sci. (U.S.A.)* 85: 1028-1032 (1988); Holt et al., *Molec. Cell. Biol.* 8: 963-973 (1988); Gerwitz et al., *Science* 242: 1303-1306 (1988); Anfossi et al., *Proc. Natl. Acad. Sci. (U.S.A.)* 86: 3379-3383 (1989); Becker et al., *EMBO J.* 8: 3685-3691 (1989)). Automated nucleic acid synthesizers may be employed for this purpose. In lieu of such synthesis, the disclosed nucleic acid molecules may be used to define a pair of primers that can be used with the polymerase chain reaction (Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.* 51: 263-273 (1986); Erlich et al., European Patent 50,424; European Patent 84,796, European Patent 258,017, European Patent 237,362; Mullis, European Patent 201,184; Mullis et al., U.S. Pat. No. 4,683,202; Erlich, U.S. Pat. No. 4,582,788; and Saiki, R. et al., U.S. Pat. No. 4,683,194) to amplify and obtain any desired nucleic acid molecule or fragment.

**[0214]** Nucleic acid molecules and fragments thereof of the present invention may also be employed to create/identify

affinity reagents which are capable of a) seeking and binding to expressed proteins and b) verifying that the protein is expressed on insect gut surface as evidenced by binding (for example, by using immunofluorescence). Examples of affinity reagents include but are not limited to RNA aptamers, high-affinity antibodies and peptide aptamers.

**[0215]** RNA aptamers are oligonucleotide ligands, usually single-stranded RNA, which have high affinity for specific proteins. RNA aptamers can be selected in vitro by the SELEX (Systemic Evolution of Ligands by Exponential Enrichment) methodology. Such methodology comprises: transcribing a DNA library; selecting RNA for binding; and reverse transcribing and amplifying over several rounds the bound RNA to produce a product capable of binding the desired target (Tuerk and Gold, *Science* 249:505-510 (1990); Gold et al., *Annu. Rev. Biochem.* 64, 763-797 (1995)).

**[0216]** Other examples of methods to generate affinity reagents include phage display technology, ribosome display technology and conventional technology for monoclonal antibodies.

**[0217]** Phage display technology refers to a selection process of phage library, which expresses a highly diverse combinatorial immunoglobulin library. The selection process involves the sequential enrichment of specific binding phage from a large excess of nonbinding clones, which is achieved by multiple rounds of phage binding to the target, washing to remove nonspecific binding phage, elution to retrieve specific binding phage and amplification of specific phage after infection of *Escherichia coli*. Any method that separates clones that bind from those that do not can be used as a selection method. Examples of selection methods includes but are not limited to biopanning on immobilized antigen on plastic plates, columns or BIAcore, or selection using biotinylated antigen. The selection and phage-retrieval methods are known to those of skill in the art and are described in the literature (for example, see Winter et al., *Annu. Rev. Immunol.* 12: 433-455 (1994); McCafferty, Hoogenboom, & Chiswell, *Antibody Engineering, a Practical Approach*. IRL Press, Oxford, UK (1996); Hoogenboom, *Trends Biotechnol.* 15: 62-70 (1997); and Griffiths et al, *EMBO J.* 13:3245-3260 (1994)).

**[0218]** Ribosome display technology refers to a methodology of phenotypic selection for ligand binding with a complete, native protein molecule in vitro (Hanes and Pluckthun, *Proc. Natl. Acad. Sci. USA* 94: 4937-4942 (1997)). Such method comprises: (1) first amplifying by PCR a DNA library, whereby introducing a T7 promoter, ribosome-binding site, and stem-loops, and then transcribing DNA to RNA; (2) translating mRNA after purification in vitro in an expression system; (3) after translation affinity-selecting desired ribosome complexes from the translation mixture by binding to the immobilized antigen and removing unspecific ribosome complexes by intensive washing; (4) dissociating the bound ribosome complexes or specifically eluting whole complexes with antigen; (5) isolating RNA from the complexes; (6) reverse transcribing isolated mRNA to cDNA and then PCR amplifying the cDNA; and (7) using the PCR amplified DNA in step 6 for the next cycle of enrichment.

**[0219]** Peptide aptamers are proteins that contain a conformationally constrained peptide region of variable sequence displayed from a scaffold. Peptide aptamers can be generated using phage display technology or ribosome display technology or conventional technology for monoclonal antibodies.